Comparison of Micro-Architectural Differences between the Breast Harboring Cancer and the Normal Contralateral Breast

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Purpose

Although the causative factors of breast cancer such as genetic mutation, endocrine, and environment are well known, there still remains a big question: why in most patients breast cancer arises unilaterally. Previous research has shown that women with extensive dense breast tissues have increased risk for developing breast cancer, and also that mammographic breast density is associated with genetic factors. Recently, it has been found that loss of heterozygosity can occur in both epithelial and stromal breast tissue adjacent to a carcinoma, and that genetic alterations in cells located in close proximity to tumor cells directly contribute to cancer progression. MRI may provide texture of breast tissues, which may be used to study architectural differences between two breasts of the same patient. However, due to the difficulty in visual assessment, quantitative analysis will be needed. In this study we applied the developed algorithms to characterize texture features extracted from MRI. Only normal breast tissues were analyzed, thus the first step was to identify and exclude lesion. An artificial neural network was applied to analyze different features between the normal tissues in the breast with cancer and the contralateral normal breast. If such a signature can be found, it may be possible to provide information to explain why the cancer grows in one side, and therein may serve as another category of risk factors associated with tumor growth. Women with these features may have a higher chance of developing breast cancer, and need to start early screening and frequent follow-up. The success will provide a more understanding about the association between breast texture with development of breast cancer.

Methods

Histological proven 21 invasive ductal carcinoma (IDC) and 16 ductal carcinoma in-situ (DCIS) cases were included in this study. In each patient, tumors were detected in only one side of breast. In the breast with cancer, the tumor was first outlined on the enhancement map and it was re-localized with boundary highlighted in the pre-contrast image as shown in Fig 1. The entire area containing the lesion and an extra layer of two-pixels outside the boundary was excluded. Then fibroglandular tissue was segmented after tumor exclusion on the pre-contrast image. As shown in Fig.1, the fat tissues show much brighter intensity and can be easily segmented by thresholding. For the other side with entirely normal tissues, the glandular tissues were directly segmented. Finally all slices from each breast were combined to obtain a 3D representation of the glandule region. The whole process of the normal tissue delineation was confirmed by an experienced radiologist. Five sets of texture analysis algorithms were applied to obtain the texture properties for each case, all together 43 texture features. They are: 9 texture features based on the gray level histogram (mean, variance, skewness, kurtosis, 1% percentile, 10% percentile. 50% percentile, 90% percentile, 99% percentile), 5 texture features based on absolute gradient (mean, variance, skewness, kurtosis, percentage of pixels with nonzero gradient), 5 run-length matrix texture features (run length nonuniformity, grey level nonuniformity, long run emphasis, short run emphasis, fraction of image in runs), 10 GLCM texture features (energy, maximum probability, contrast, homogeneity, entropy, correlation, sum average, sum variance, difference average, and difference variance) and 14 LAWS' texture energy features. Since many features in the data set are usually irrelevant and redundant with each other, artificial neural network (ANN) was used to identify different features which can best discriminate between the breast with cancer and the breast without cancer. The multiple layer perceptron (MLP) network was used as classification method and due to the limited sample size the leave-one-out cross validation was used to evaluate the generated classifier. Finally the classification accuracy was compared using the ROC analysis.

Results

The ANN classification based on 43 texture features can achieve up 81% accuracy (area under the ROC curve) to differentiate between breast with DCIS and the contralateral breast. The differentiation in cases with IDC only reached 69% as shown in Fig.2. For DCIS cases, the selected classification features included 1 GLCM (difference variance), 4 Laws' (LAW_LE, LAW_LS, LAW_EE, LAW_ES) features, 2 histogram features (Variance, 50% percentile). During the search of the best topologic structure, we found that LAW's texture features had extremely high chance to be selected, especially for LAW_LE, LAW_LS. Paired t-test was also used to investigate the performance of individual parameter. 12/14 LAW's features show significant differences between the breast with/without cancer (p=0.00001~0.004). The results suggested that LAW's features might be the most relevant features. Fig. 1 shows how the tumor region was segmented off. Fig. 2 shows the ROC curves from ANN analysis for both DCIS and IDC.

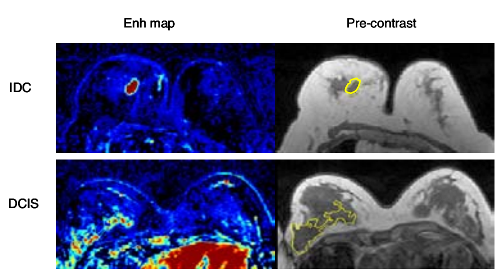

Fig.1 Two cases of IDC and DCIS illustrating the process of tumor extraction. After localized tumor in enhancement map, lesion with highlighted boundary was shown in pre-contrast image. Fibroglandular tissue then can be manually outlined without infiltrating the tumor.

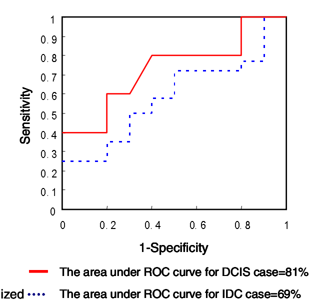

Fig.2 The ROC curves from ANN analysis

Discussion

Using a powerful neural training classification algorithm we selected a subset of MRI texture features which can differentiate between the normal tissues in the breast harboring DCIS compared to the normal tissues in the contralateral breast. The area under ROC was 81%. When the sensitivity was set at 80%, the specificity was 60%. Since this is only to provide a risk factor for alerting patients to start early screening, a low specificity was not a great concern. The different texture might be associated with stochastic genetic mutations and other mechanisms such as atypical ductal hyperplasia and pathophysiological changes of the mammary glandular trees. Women with these features may have a higher chance of developing breast cancer and need to start early screening and frequent follow-up. In this pilot study with a small case number, we have demonstrated the feasibility to analyze texture of fibroglandular tissues. When more cases are added, the power of training could be greatly improved, and at that time we may be able to further compare between IDC and DCIS cases.

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